Complete Summary

GUIDELINE TITLE

Prevention of herpes zoster. Recommendations of the Advisory Committee on Immunization Practices (ACIP).

BIBLIOGRAPHIC SOURCE(S)

Harpaz R, Ortega-Sanchez IR, Seward JF, Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention. Prevention of herpes zoster. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2008 Jun 6;57(RR-5):1-30; quiz CE2-4. [224 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Herpes zoster (shingles)

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Dermatology
Family Practice
Geriatrics
Infectious Diseases
Internal Medicine
Pharmacology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To provide recommendations on the use of a live attenuated vaccine for the prevention of herpes zoster

TARGET POPULATION

Adults ≥60 years in the United States

INTERVENTIONS AND PRACTICES CONSIDERED

Herpes zoster (zoster) vaccination with live attenuated vaccine

- Routine vaccination of persons aged ≥60 years
- Simultaneous administration with other adult vaccines
- Special groups and circumstances
    - Persons with a reported history of zoster, anticipating immunosuppression, receiving antiviral medications or blood products, and nursing mothers

MAJOR OUTCOMES CONSIDERED

- Incidence of herpes zoster (zoster)
- Incidence of postherpetic neuralgia
- Incidence of recurrent zoster
- Zoster-related hospitalization rates
- Zoster-related morbidity and mortality rates
- Quality of life
- Zoster vaccine-related adverse events
- Cost effectiveness of zoster vaccine

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In September 2005, the Advisory Committee on Immunization Practices (ACIP) measles-mumps-rubella and varicella workgroup expanded its membership to include experts in adult medicine and in zoster and began review of relevant data on zoster and the investigational vaccine. Shortly thereafter, this workgroup reformed as the ACIP shingles workgroup and, during subsequent months, held 19 conference calls to review and discuss scientific evidence related to herpes zoster and zoster vaccine, including the epidemiology and natural history of zoster and its sequelae, and the safety, immunogenicity, efficacy, financing, storage, and handling of the zoster vaccine. The workgroup also reviewed several economic analyses on zoster prevention. Workgroup members participated in 10 additional conference calls to develop and discuss recommendation options for preventing

zoster. When scientific evidence was lacking, recommendations incorporated expert opinions of the workgroup members.

Presentations of background materials on zoster and the vaccine were made during ACIP meetings in October 2005 and the three meetings in 2006. Following vaccine licensure on May 25, 2006, recommendation options were presented to ACIP in June 2006, and final options were presented at the October 2006 meeting. During review by the Centers for Disease Control and Prevention (CDC) and external partners, modifications were made to the proposed recommendations to update and clarify wording in the document. As new information on the epidemiology and prevention of zoster becomes available, it will be reviewed by ACIP and recommendations will be updated as needed.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The economic burden of zoster in the elderly is substantial and includes direct costs attributed to health-care use and indirect costs attributed to losses in productivity from temporary or more permanent disability. In addition, much of the economic burden of zoster is borne by individual patients as reduced quality of life because of pain and suffering. Certain studies provide a range of estimates for health-care use among persons aged $\geq$60 years for treatment of zoster and postherpetic neuralgia (PHN). The estimates vary widely because of differing assumptions regarding the risk for PHN and of complications resulting from zoster. Estimated health-care use per case of zoster ranges from 1.3 to 3.1 for the number of outpatient visits, 0.005 to 0.12 for the number of emergency department visits, and 1 to 5 for the number of medications prescribed. Approximately 1 to 4% of zoster episodes result in hospitalization, with a mean duration of 4.8 days. Health-care use for zoster and PHN increases substantially with the age of patients.

Costs associated with acute zoster have been evaluated. Among patients with acute episodes of zoster, average expenditures ranged from $112 to $287 per episode of out-patient care, $73 to $180 per antiviral treatment, and $3,221 to $7,206 per hospitalization (2006 dollars). Additional costs associated with managing non-PHN complications (e.g., ocular, neurologic, and cutaneous) ranged from $1,158 to $11,255 per complication, and from $566 to $1,914 per episode of PHN. Among the subset of patients with PHN persisting from 30 days to 12 months, annualized health-care costs, including costs of the acute episode, ranged from $2,159 to $5,387. Although indirect costs from death can occur with zoster, these costs result mostly from losses in work time caused by temporary or more permanent disability. Patients with zoster (including those progressing to PHN) lose an average of >129 hours of work per episode, including losses of 12 or more hours of work time and 69 hours of leisure time during the first 30 days. Data on the national economic impacts of zoster and its complications on quality of life have not been reported.

Five studies have estimated the cost-effectiveness of a 1-dose routine vaccination program of immunocompetent persons aged $\geq$60 years (see Table 5 in the

original guideline document). One of these studies has not been published. All five studies used a Markov cohort model, followed a cost-utility analytic approach that included a societal perspective, and used quality-adjusted life-year (QALY) scores to assess the incremental impact of the vaccine program on quality of life. Costs and health benefits were measured in 2005 to 2006 U.S. dollars, and a 3% discount rate was used to adjust health outcomes and costs. Model assumptions varied regarding duration of vaccine protection, the efficacy of the vaccine for preventing PHN among vaccine recipients who developed zoster, costs associated with vaccine adverse events, and costs attributed to losses in work productivity. None of the five models incorporated costs for losses in leisure time. Assuming a routine vaccination program with 100% coverage, the estimated QALYs gained ranged from 0.0016 (0.6 days) to 0.0087 (3 days). At a vaccine cost of $150 per dose, the societal costs of routinely vaccinating immunocompetent persons aged ≥60 years range from $27,000 to $112,000 per QALY gained. In the sensitivity analyses, variables with the strongest influence on outcomes include vaccine costs, duration of vaccine efficacy, risks for PHN as a complication, and costs and QALY scores for zoster and its complications.

Although costs per QALY gained are most appropriately used to prioritize among competing programs for purposes of resource allocation, policymakers often decide whether or not to support programs by comparing their cost per QALY against a standard threshold. A threshold suggested by the World Health Organization is three times the gross domestic product per capita, which would be $94,431 for the United States. Alternatively, policymakers often decide about supporting programs by comparing their cost per QALY with the values for other widely accepted interventions. Compilations of such cost effectiveness data have been published and maintained in on-line registries. The estimated cost per QALY for zoster vaccination covers a wide range that appears acceptable in comparison to either standard thresholds or to other established interventions, but it is at the intermediate-to-high end of that range.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

These recommendations were presented to the full Advisory Committee on Immunization Practices (ACIP) and approved in October 2006. Modifications were made to the ACIP statement during the subsequent review process at the Centers for Disease Control and Prevention (CDC) to update and clarify wording in the document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Routine Vaccination of Persons Aged >60 Years

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of all persons aged ≥60 years with 1 dose of zoster vaccine. Persons

who report a previous episode of zoster and persons with chronic medical conditions (e.g., chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease) can be vaccinated unless those conditions are contraindications or precautions. Zoster vaccination is not indicated to treat acute zoster, to prevent persons with acute zoster from developing postherpetic neuralgia (PHN), or to treat ongoing PHN. Before routine administration of zoster vaccine, it is not necessary to ask patients about their history of varicella (chickenpox) or to conduct serologic testing for varicella immunity.

Simultaneous Administration with Other Adult Vaccines

Immunogenicity of zoster vaccine and trivalent inactivated influenza vaccine is not compromised when the two vaccines are administered simultaneously. However, no data exist on administration of zoster vaccine with other vaccines routinely recommended for persons aged ≥60 years, which are all inactivated. In general, the simultaneous administration of most widely used live, attenuated and inactivated vaccines has not resulted in impaired immune response or an increased rate of adverse events. Therefore, zoster vaccine can be administered with other indicated vaccines during the same visit (e.g., tetanus and reduced diphtheria toxoids [Td], tetanus, reduced diphtheria, and acellular pertussis [Tdap], and pneumococcal polysaccharide vaccines). Each vaccine must be administered using a separate syringe at a different anatomic site. If simultaneous administration is not possible, zoster vaccine can be administered at any time before or after an inactivated vaccine, but at least 4 weeks before or after another live, attenuated vaccine.

Groups for Which Vaccine is Not Licensed

Vaccination of Persons Aged <60 Years

The vaccine is not licensed for persons aged <60 years, and no recommendation exists for routine vaccination of persons aged <60 years. In the clinical trial, the zoster vaccine was evaluated among persons aged ≥60 years. The vaccine was most effective and well tolerated in the youngest persons (see Table 1 in the original guideline document). Although the vaccine would probably be safe and effective in persons aged <60 years, data are insufficient to recommend vaccination of these persons at this time.

Vaccination of Persons Who Have Received Varicella Vaccine

Zoster vaccination is not recommended for persons of any age who have received varicella vaccine. However, health-care providers do not need to inquire about varicella vaccination history before administering zoster vaccine because virtually all persons currently or soon to be in the recommended age group have not received varicella vaccine. In the United States, varicella vaccination began in 1995. Since that time, few adults aged ≥40 years would have been susceptible to varicella and thus eligible to receive varicella vaccine. The number of persons eligible for zoster vaccination who have received varicella vaccine is extremely small and will remain so for at least a decade.

Special Groups and Circumstances

Persons with a Reported History of Zoster

Persons with a reported history of zoster can be vaccinated. Repeated zoster has been confirmed in immunocompetent persons soon after a previous episode. Although the precise risk for and severity of zoster as a function of time following an earlier episode are unknown, some studies suggest it may be comparable to the risk in persons without a history of zoster. Furthermore, no laboratory evaluations exist to test for the previous occurrence of zoster, and any reported diagnosis or history might be erroneous. Although the safety and efficacy of zoster vaccine have not been assessed in persons with a history of zoster, different safety concerns are not expected in this group.

Persons Anticipating Immunosuppression

The risk for zoster and its severe morbidity and mortality is much greater among persons who are immunosuppressed. Review of vaccination status for zoster and other vaccines should be a key component of the medical assessment for immunocompetent patients aged $\geq$60 years who might be anticipating initiation of immunosuppressive treatments or who have diseases that might lead to immunodeficiency. Such patients without a history of zoster vaccination should receive 1 dose of zoster vaccine at the first possible clinical encounter while their immunity is intact. Zoster vaccine should be administered at least 14 days before initiation of immunosuppressive therapy, although some experts advise waiting 1 month after zoster vaccination to begin immunosuppressive therapy if delay is possible.

Persons Receiving Antiviral Medications

Licensed antiviral medications active against members of the herpesvirus family include acyclovir, famciclovir, and valacyclovir. These agents might interfere with replication of the live, varicella zoster virus (VZV)-based zoster vaccine. All three agents have relatively short serum half-lives and are quickly cleared from the body. Persons taking chronic acyclovir, famciclovir, or valacyclovir should discontinue these medications at least 24 hours before administration of zoster vaccine, if possible. These medications should not be used for at least 14 days after vaccination, by which time the immunologic effect should be established.

Persons Receiving Blood Products

Zoster vaccine can be administered to persons at any time before, concurrent with, or after receiving blood or other antibody-containing blood product because persons with a history of varicella indefinitely maintain high levels of antibody to VZV, and the levels are comparable to those found in donated blood and antibody-containing blood products (e.g., whole blood, packed red blood cells, and plasma immune globulin, hyperimmune globulin, and intravenous immune globulin).

Nursing Mothers

Most live vaccines, including varicella vaccine, are not secreted in breast milk. Therefore, breast feeding is not a contraindication for zoster vaccination.

However, this situation will be extremely rare in the target age group for this vaccine.

Contraindications

Allergy to Vaccine Components

Zoster vaccine is contraindicated for persons who have a history of anaphylactic reaction to any component of the vaccine, including gelatin and neomycin. Neomycin allergy is usually manifested as a contact dermatitis, which represents a delayed-type immune response. A history of contact dermatitis to neomycin is not a contraindication for receiving zoster vaccine.

Immunocompromised Persons

Zoster vaccine should not be administered to persons with primary or acquired immunodeficiency including:

- Persons with leukemia, lymphomas, or other malignant neoplasms affecting the bone marrow or lymphatic system. However, patients whose leukemia is in remission and who have not received chemotherapy (e.g., alkylating drugs or antimetabolites) or radiation for at least 3 months can receive zoster vaccine.
- Persons with acquired immune deficiency syndrome (AIDS) or other clinical manifestations of human immunodeficiency virus (HIV), including persons with CD4+ T-lymphocyte values $\leq$200 per mm^3 or $\leq$15% of total lymphocytes.
- Persons on immunosuppressive therapy, including high-dose corticosteroids ($\geq$20 mg/day of prednisone or equivalent) lasting two or more weeks. Zoster vaccination should be deferred for at least 1 month after discontinuation of such therapy. Short-term corticosteroid therapy (<14 days); low-to-moderate dose (<20 mg/day of prednisone or equivalent); topical (e.g., nasal, skin, inhaled); intra-articular, bursal, or tendon injections; or long-term alternate-day treatment with low to moderate doses of short-acting systemic corticosteroids are not considered to be sufficiently immunosuppressive to cause concerns for vaccine safety. Persons receiving this dose or schedule can receive zoster vaccine. Therapy with low-doses of methotrexate ($\leq$0.4 mg/Kg/week), azathioprine ($\leq$3.0 mg/Kg/day), or 6 mercaptopurine ($\leq$1.5 mg/Kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease, and other conditions are also not considered sufficiently immunosuppressive to create vaccine safety concerns and are not contraindications for administration of zoster vaccine.
- Persons with clinical or laboratory evidence of other unspecified cellular immunodeficiency. However, persons with impaired humoral immunity (e.g., hypogammaglobulinemia or dysgammaglobulinemia) can receive zoster vaccine.
- Persons undergoing hematopoietic stem cell transplantation (HSCT). The experience of HSCT recipients with VZV-containing vaccines (e.g., zoster vaccine) is limited. Physicians should assess the immune status of the recipient on a case-by-case basis to determine the relevant risks. If a decision is made to vaccinate with zoster vaccine, the vaccine should be administered at least 24 months after transplantation.

- Persons receiving recombinant human immune mediators and immune modulators, especially the antitumor necrosis factor agents adalimumab, infliximab, and etanercept. The safety and efficacy of zoster vaccine administered concurrently with these agents is unknown. If it is not possible to administer zoster vaccine to patients before initiation of therapy, physicians should assess the immune status of the recipient on a case-by-case basis to determine the relevant risks and benefits. Otherwise, vaccination with zoster vaccine should be deferred for at least 1 month after discontinuation of such therapy.

Pregnancy

Zoster vaccine is not recommended for use in pregnant women, although these women are unlikely to be in the vaccine target age group. The effects of the live, attenuated VZV-based zoster vaccine on the fetus are unknown. Women should avoid becoming pregnant for 4 weeks following zoster vaccination. Having a pregnant household member is not a contraindication to zoster vaccination. If a pregnant woman is vaccinated or becomes pregnant within 1 month of vaccination, she should be counseled about potential effects on the fetus. Wild-type VZV poses a small risk to the fetus, and the fetal risk from the attenuated zoster vaccine is probably even lower. Furthermore, virtually all persons receiving the vaccine will have preexisting VZV immunity, which is expected to limit viral replication and presumably further reduce fetal risk. In most circumstances, the decision to terminate a pregnancy should not be based on whether zoster vaccine was administered during pregnancy. Merck & Co., Inc., in collaboration with Centers for Disease Control and Prevention (CDC), has established a pregnancy registry to monitor the maternal-fetal outcomes of pregnant women who are inadvertently administered live-attenuated VZV-based vaccines within 1 month of pregnancy (telephone: 800-986-8999). Patients and health-care providers should report any exposure to zoster vaccine during pregnancy to this registry.

Precautions

Moderate to Severe Illness

Zoster vaccination of persons who have severe acute illness should be postponed until recovery. The decision to delay vaccination depends on the severity of symptoms and the etiology of the disease. Zoster vaccine can be administered to persons who have mild acute illnesses with or without fever.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved vaccination coverage levels
- Appropriate use of herpes zoster vaccine
- Decreased burden of herpes zoster and its complications among persons with high levels of risk

POTENTIAL HARMS

Serious Adverse Events

Adverse events were monitored in the Shingles Prevention Study population, with more comprehensive ascertainment in a safety substudy comprising 6,616 persons (3,345 vaccine recipients and 3,271 placebo recipients) (see Table 4 in the original guideline document). In the Shingles Prevention Study population, the number and types of serious adverse events during the 42 days after receipt of vaccine or placebo were similar (1.4%). However, rates of serious adverse events in the safety substudy were higher in vaccine recipients (1.9%) than in placebo recipients (1.3%), with a relative risk of 1.5 (95% confidence interval [CI] = 1.0–2.3). Nonetheless, no temporal or clinical patterns of adverse events were observed in vaccine recipients to suggest a causal relation. The incidence of death and hospitalizations was similar in the two treatment groups throughout the observation time.

Mild Local and Systemic Reactions

In the Shingles Prevention Study safety substudy, self-reported injection site adverse events (e.g., erythema, pain, swelling, warmth, and pruritis) were more common among vaccine recipients (48.3%) than placebo recipients (16.6%) ($p<0.05$) (see Table 4 in the original guideline document); the risk for these events was higher in vaccine recipients aged 60–69 years (58.3%) than in persons aged $\geq$70 years (41.3%). Most injection site adverse events were mild and resolved within 4 days. Less-serious systemic adverse events, including headaches, were more common in vaccine recipients (6.3%) than in placebo recipients (4.9%) ($p<0.05$) (see Table 4 in the original guideline document). The risk for fevers after vaccination did not differ between vaccine recipients and controls.

The safety and tolerability of zoster vaccine was evaluated in a separate study among persons aged 50 to 59 years, including 62 persons who received the standard potency (approximately 58,000 PFUs) and 123 persons who received high potency (approximately 207,000 PFUs). Although the numbers of persons was small, both vaccines were safe and well tolerated; however, injection site reactions were more common (69.4% and 82.9%, respectively) than those observed in person aged >60 years in the Shingles Prevention Study (48.3%).

Vaccine Virus Rash and Transmission

Varicella-like rashes, including injection site varicella-like lesions, generalized varicella-like rashes, and zoster-like rashes, were evaluated in the Shingles Prevention Study during the first 42 days of observation (see Table 4 in the original guideline document). Twenty vaccine recipients and seven placebo recipients had lesions at the injection site ($p<0.05$); the lesions were tested for varicella zoster virus (VZV) by polymerase chain reaction (PCR) in one of these persons in each group, and results were negative in both. Among the vaccine recipients, lesions occurred a median of 3 to 4 days after vaccination and lasted a median of 5 days.

Generalized varicella-like rashes occurred at similar rates in the two groups (see Table 4 in the original guideline document). Zoster-like rashes were less common in vaccine versus placebo recipients during this 42-day period ($p<0.05$).

Oka/Merck strain VZV was not detected in any of 10 lesion specimens from vaccine recipients available for PCR testing. In early studies conducted as part of the manufacturer's clinical program for development of zoster vaccine, samples from rashes in two vaccinated persons were confirmed to be Oka/Merck-strain VZV. Both experienced noninjection-site varicella-like rashes; one had 21 lesions on day 17 lasting 8 days and the other developed five lesions on day 8 that lasted 16 days. No varicella-like rashes were documented during any clinical zoster vaccine trials of laboratory-confirmed zoster attributed to Oka/Merck strain VZV. In addition, no evidence existed of transmission of vaccine virus from vaccine recipients to contacts.

Administration Errors

The zoster vaccine, ZOSTAVAX®, is a live, attenuated vaccine containing Oka/Merck strain VZV. The vaccine is similar to the varicella vaccine, VARIVAX®, except the minimum PFU-content of the ZOSTAVAX® is at least 14-fold higher than the minimum PFU-content of VARIVAX®. Opportunities for administration errors are possible.

Risk for Transmission of Oka/Merck Strain After Receiving Zoster Vaccine

Persons having close household or occupational contact with persons at risk for severe varicella need not take any precautions after receiving zoster vaccine except in rare instances in which a varicella-like rash develops, when standard contact precautions are adequate. Although transmission of Oka/Merck strain VZV has been documented following varicella vaccination, such transmission is rare and has only been documented when the vaccine recipient first developed a varicella-like rash. Rates of varicella-like rash appear to be less common following zoster vaccination than following varicella vaccination, and transmission of the Oka/Merck strain VZV from recipients of zoster vaccine has not been detected. The risk for transmitting the attenuated vaccine virus to susceptible persons should be weighed against the risk for developing wild-type zoster that could be transmitted to a susceptible person.

CONTRAINDICATIONS

CONTRAINDICATIONS

See the "Major Recommendations" field for contraindications to the zoster vaccine.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This report does not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of the discussion of off-label use of zoster vaccine by persons who report a previous episode of herpes zoster. In addition, guidance is provided for instances in which zoster vaccine is inadvertently administered.
- Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.
- References to non-Centers for Disease Control and Prevention (CDC) sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of these sites. URL addresses listed in *MMWR* were current as of the date of publication.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Program Implementation Issues

Following Good Adult Vaccination Practices

Zoster vaccine should be offered to patients aged ≥60 years at the first available clinical encounter with their provider. The average adult in this age group has 5 to 8 clinical encounters with their provider annually. Strategies to promote zoster vaccination include linking delivery of zoster vaccine to delivery of other indicated adult vaccines (e.g., influenza) and preventive-health interventions, standing orders so that patients will automatically be offered indicated vaccines rather than requiring case-by-case physicians' orders, and practice-based audits and/or physician-reminder systems. Residents of nursing homes and other long-term–care facilities who are at least aged 60 years and without contraindications should be included in routine zoster vaccination activities. When administering zoster vaccine, health-care providers should review the patient's vaccination status for all indicated adult vaccines.

The Advisory Committee on Immunization Practices (ACIP) recommends that health-care providers keep permanent documentation of all administered vaccines, including zoster vaccine, in the vaccine recipient's permanent medical record. The type of the vaccine, manufacturer, anatomic site, route of delivery, date of administration, lot number, and name of the administering facility should be recorded. To help avoid the administration of unnecessary doses, every patient should be given a record of the vaccination.

Administration Errors

The zoster vaccine, ZOSTAVAX®, is a live, attenuated vaccine containing Oka/Merck strain varicella zoster virus (VZV). The vaccine is similar to the varicella vaccine, VARIVAX®, except the minimum PFU-content of the ZOSTAVAX® is at least 14-fold higher than the minimum PFU-content of VARIVAX®. Opportunities for administration errors are possible.

For providers who serve both children and adults, physical separation of products, careful visual inspection and reading of labels, and preparation of vaccine for patient use only at time of vaccination can help prevent errors. If a provider mistakenly administers high-potency zoster vaccine to a child indicated for varicella vaccine, the level of protection against varicella would probably be at least the same as for conventional doses of varicella vaccine. This erroneous dose should count as a single valid dose of varicella vaccine. If the erroneous dose was administered in lieu of the first dose of varicella vaccine, a second dose of varicella vaccine is required. Administration errors involving zoster vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS) whether or not an adverse event occurs.

Early clinical trials for prevention of varicella were conducted in susceptible children using a formulation of live-attenuated Oka/Merck strain VZV at doses of 17,430 PFU, approaching the range of PFU in zoster vaccine ($\geq$19,400 PFU). This high-dose formulation was well tolerated and efficacious. The more recently licensed live, attenuated Oka-strain varicella zoster virus (VZV) vaccine (PROQUAD®) prepared in combination with measles, mumps, and rubella vaccine (MMRV) is formulated with a broad range of titers that extend to over 60,000 PFU.

Varicella vaccine (VARIVAX®) is not indicated for prevention of zoster. MMRV vaccine (PROQUAD®) is not licensed for use in persons aged $\geq$13 years. If a provider mistakenly administers varicella vaccine to persons indicated for zoster vaccine, no specific safety concerns exists, but the dose should not be considered valid and the patient should be administered a dose of zoster vaccine during that same visit. If the error is not immediately detected, a dose of zoster vaccine should be administered as soon as possible but not within 28 days of the varicella vaccine dose to prevent potential interference of 2 doses of live attenuated virus.

Risk for Transmission of Oka/Merck Strain After Receiving Zoster Vaccine

Persons having close household or occupational contact with persons at risk for severe varicella need not take any precautions after receiving zoster vaccine except in rare instances in which a varicella-like rash develops, when standard contact precautions are adequate. Although transmission of Oka/Merck strain VZV has been documented following varicella vaccination, such transmission is rare and has only been documented when the vaccine recipient first developed a varicella-like rash. Rates of varicella-like rash appear to be less common following zoster vaccination than following varicella vaccination, and transmission of the Oka/Merck strain VZV from recipients of zoster vaccine has not been detected. The risk for transmitting the attenuated vaccine virus to susceptible persons should be weighed against the risk for developing wild-type zoster that could be transmitted to a susceptible person. If a susceptible, immunocompromised person is inadvertently exposed to a person who has a vaccine-related rash, VARIZIG™

need not be administered because disease associated with this type of transmission is expected to be mild. Acyclovir, valacyclovir, and famciclovir are active against live-attenuated Oka/Merck strain VZV and can be used in the unlikely situations in which a severe illness develops in the susceptible contact.

Reporting of Adverse Events after Vaccination

As with any newly licensed vaccine, surveillance for rare adverse events associated with administration of zoster vaccine is important for assessing its safety in widespread use. Vaccine safety surveillance in the age group for which zoster vaccine is recommended (aged ≥60 years) will present challenges because of the high prevalence of chronic conditions, the frequent use of multiple medications, and the common occurrence of medical events. Coincident adverse events can be anticipated following zoster vaccination, but many of these could be caused by the vaccine as well. All clinically significant adverse events should be reported to VAERS even if causal relation to vaccination is not certain. VAERS reporting forms and information are available electronically at http://www.vaers.hhs.gov or by telephone (800-822-7967). Web-based reporting is also available, and providers are encouraged to report electronically at https://secure.vaers.org/VaersDataEntryintro.htm.

IMPLEMENTATION TOOLS

Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Harpaz R, Ortega-Sanchez IR, Seward JF, Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention. Prevention of herpes zoster. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2008 Jun 6;57(RR-5):1-30; quiz CE2-4. [224 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 Jun 6

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Advisory Committee on Immunization Practices Shingles Work Group

Advisory Committee on Immunization Practices

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Advisory Committee on Immunization Practices Shingles Work Group

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